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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/304,564	05/04/1999	MOHAMED CHOKRI	USD-93-AG-ID	9853
466	7590	12/19/2003	EXAMINER	
YOUNG & THOMPSON 745 SOUTH 23RD STREET 2ND FLOOR ARLINGTON, VA 22202			HOLLERAN, ANNE L	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 12/19/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/304,564

Applicant(s)

CHOKRI ET AL.

Examiner

Anne Holleran

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 May 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. In view of a new art rejection, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

Claim Rejections Withdrawn:

2. The rejection of claims 3-5 under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention is withdrawn upon further consideration.

Claim Rejections Maintained and New Grounds of Rejection:

3. The rejection of claims 3-5 under 35 U.S.C. 102(b) as being anticipated by Chokri (Chokri, M. et al., Res. Immunol., 143: 95-99, 1992) is maintained for the reasons of record.

Chokri teach a method of treating tumors by administration of macrophages and bispecific antibodies that recognize both the FcγRI of macrophages and recognizes human

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adenocarcinoma antigen (see abstract). The macrophages increase cytotoxic activity compared to standard macrophages by about 20-40 percent in the presence of interferon-gamma (see Table II, page 98). Chokri teaches precoating the macrophages with bispecific antibodies (preincubation of macrophages) and simultaneous administration of macrophages and bispecific antibodies (see page 97, 2nd column). Thus, Chokri teaches methods that are the same as that claimed.

Applicants have argued that Chokri fails to teach the same macrophages used in the claimed methods, and therefore, fails to anticipate the claimed methods. This argument is unpersuasive, because with respect to claimed macrophages that, in the presence of interferon-gamma, have increased cytotoxic activity with respect to standard macrophages by about 20-40 percent, Chokri does teach such macrophages in Table II, page 98. These macrophages are within the scope of those recited in the claimed methods, because the claimed methods do not recite that the standard macrophages are also in the presence of interferon-gamma. The specification broadly defines standard macrophages as ones obtained by culture of monocytes in a standard medium. This rejection would be withdrawn if applicants were to amend the claims to recite “-their cytotoxic activity with IFN- γ is increased by about 20 to about 40% with respect to standard macrophages incubated with IFN- γ ;”.

4. The rejection of claims 3-5 under 35 U.S.C. 102(e) as being anticipated by Fanger (U.S. Patent 5,635,600; issued June 3, 1997; effective filing date Feb. 2, 1988) is maintained for the reasons of record.

Fanger discloses method of treating cancer by administering bispecific antibodies and macrophages (col. 5, lines 17-28, and col. 5, line 61-col. 6, line 27), where the macrophages may be armed with bispecific antibodies (reads on simultaneous administration and preincubation of macrophages with bispecific antibodies). The macrophages may be treated with interferon-gamma. Absent evidence to the contrary, the macrophages of Fanger will exhibit the same characteristics that are listed in claim 3 for activation of macrophages by interferon-gamma. Thus, Fanger discloses methods that are the same as that claimed.

Applicants have argued that Fanger fails to teach the same macrophages used in the claimed methods, and therefore, fails to anticipate the claimed methods. This argument is unpersuasive, because with respect to claimed macrophages that, in the presence of interferon-gamma, have increased cytotoxic activity with respect to standard macrophages by about 20-40 percent, Fanger teaches macrophages that may be treated with interferon-gamma. These macrophages are within the scope of those recited in the claimed methods, because the claimed methods do not recite that the standard macrophages are also in the presence of interferon-gamma. The specification defines standard macrophages as ones obtained by culture of monocytes in a standard medium. This rejection would be withdrawn if applicants were to amend the claims to recite “-their cytotoxic activity with IFN- γ is increased by about 20 to about 40% with respect to standard macrophages incubated in the presence of IFN- γ ;”.

5. The rejection of claims 3-5 under 35 U.S.C. 102(b) as being anticipated by Medarex (WO 91/05871; published May 2, 1991) is maintained for the reasons of record.

Medarex teaches method for treating cancer by administering bispecific antibodies and macrophages (page 5, lines 5-21; page 6, line 19 to page 7, line 3), where the macrophages may be armed with bispecific antibodies (reads on simultaneous administration and preincubation of macrophages). The macrophages may be treated with interferon-gamma. Absent evidence to the contrary, the macrophages of Medarex will exhibit the same characteristics that are listed in claim 3 for activation of macrophages by interferon-gamma. Thus, Medarex teaches methods that are the same as that claimed.

Applicants have argued that Medarex fails to teach the same macrophages used in the claimed methods, and therefore, fails to anticipate the claimed methods. This argument is unpersuasive, because with respect to claimed macrophages that, in the presence of interferon-gamma, have increased cytotoxic activity with respect to standard macrophages by about 20-40 percent, Medarex teaches macrophages that may be treated with interferon-gamma. These macrophages are within the scope of those recited in the claimed methods, because the claimed methods do not recite that the standard macrophages are also in the presence of interferon-gamma. The specification defines standard macrophages as ones obtained by culture of monocytes in a standard medium. This rejection would be withdrawn if applicants were to amend the claims to recite “-their cytotoxic activity with IFN- γ is increased by about 20 to about 40% with respect to standard macrophages incubated in the presence of IFN- γ ;”.

Double-Patenting:

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed.

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Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

6. Claims 3-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 6,540,994 in view of Chokri (supra, "Chokri I"), Fanger (supra) or Medarex (supra). Claims 3-5 are drawn to methods for treating cancer comprising administering macrophages and bispecific antibodies. Claims 1 and 3 are drawn to methods of treatment comprising administering the same macrophages as recited in claims 3-5 of the instant application. Claims 1 and 3 of U.S. Patent 6,540,994 differ from the instant claims in that the claims 1 and 3 are drawn methods where the macrophages are combined with lymphocytes, but are not necessarily administered with bispecific antibodies, whereas the instant claims require the administration of bispecific antibodies. However, the methods of claims 1 and 3 of U.S. Patent 6,540,994 encompass methods where the combined macrophage plus lymphocyte preparation are administered in the presence of bispecific antibodies. Co-administration with bispecific antibodies is within the scope of claims 1-3. The prior art teaches the advantages of methods of treatment that comprise the administration with bispecific antibodies with immune cell preparations. Therefore, the combination of bispecific antibodies with the macrophage-lymphocyte preparation recited in claim 1 is an obvious species of the genus of claims 1 and 3.

7. Claims 3-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chokri II (Anticancer Res. 1992, Vol. 12, pages 2257-2260; cited in the IDS) in view of either Chokri (supra, "Chokri I"), Fanger (supra) or Medarex (supra).

Chokri II teaches macrophages that are identical to the macrophages recited in the claimed methods. Chokri II suggests the in vivo administration of a composition of said macrophages to a patient.

Chokri II fails to teach a method where the macrophages are administered together with bispecific antibodies.

However, Chokri I teaches methods of administering macrophages in the presence of bispecific antibodies (arming the macrophages), as does Fanger and Medarex. All of these references individually teach the advantages of treating a patient with armed immune effector cells.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made that the macrophages of Chokri II could be armed with bispecific antibodies to make the claimed methods of treatment.

It is noted that the publication date of Chokri II is less than one year from the effective filing date of the instant application. However, the authorship of Chokri II falls under the category of "another inventor", because it names inventors that are not named as co-inventors in the instant application. MPEP 2132 defines "another inventor" as any combination of authors or inventors different than the inventive entity of the application. The term "another" in 35 U.S.C. 102(a) refers to any entity which is different from the inventive entity. The entity need only differ by one person to be "by another".

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Office should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:30 am to 2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

Anne L. Holleran
Patent Examiner
December 3, 2003

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